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**United States Patent** [19]**Shah et al.**[11] **Patent Number:** **6,039,975**[45] **Date of Patent:** **Mar. 21, 2000**[54] **COLON TARGETED DELIVERY SYSTEM**[75] Inventors: **Navnit Hargovindas Shah; Aruna M. Raikar**, both of Clifton; **Wantanee Phuapradit**, Jersey City, all of N.J.[73] Assignee: **Hoffman-La Roche Inc.**, Nutley, N.J.[21] Appl. No.: **08/717,032**[22] Filed: **Sep. 20, 1996****Related U.S. Application Data**

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[51] **Int. Cl.<sup>7</sup>** ..... **A61K 9/24**[52] **U.S. Cl.** ..... **424/473; 424/472**[58] **Field of Search** ..... **424/472, 473**[56] **References Cited****U.S. PATENT DOCUMENTS**

4,609,374	9/1986	Ayer	.....	424/473
4,668,517	5/1987	Weber et al.	.	
4,871,549	10/1989	Ueda et al.	.	
4,891,223	1/1990	Ambegaonkar et al.	.....	424/473
5,171,580	12/1992	Iamartino et al.	.	
5,225,202	7/1993	Hodges et al.	.	

**FOREIGN PATENT DOCUMENTS**

0148811	7/1985	European Pat. Off.	.....	424/473
1804736	6/1969	Germany	.....	424/472

**OTHER PUBLICATIONS**

W. Phuapradit, et al, In Vitro Characterization Of Polymeric Membrane Used For Controlled Release Application, Drug Development and Industrial Pharmacy, vol. 21(8) pp. 955-963 (1995).

S.S. Rao, et al, Development And In Vitro/In Vivo Evaluation Of A Colonic Release Capsule Of Vasopressin, International Journal Of Pharmaceutics, vol. 86 pp. 35-41 (1992).

D. Friend, et al, A Colon-Specific Drug-Delivery System Based On Drug Glycosides And The Glycosidases Of Colonic Bacteria, J. Med. Chem. vol. 27 pp. 261-266 (1984).

C. Larsen, et al, Macromolecular Prodrugs. XVI. Colon-Targeted Delivery-Comparison Of The Rate Of Release Of Naproxen From Dextran Ester Prodrugs In Homogenates Of Various Segments Of The Pig Gastrointestinal (GI) Tract, Pharmaceutical Research, vol. 6, No. 12 pp. 995-999 (1989).

M.J. Dew, et al, An Oral Preparation To Release Drugs In The Human Colon, British Journal of Clinical Pharmacology, vol. 14 pp. 405-408 (1982).

J.G. Hardy, et al, Drug Delivery To the Proximal Colon, J. Pharm. Pharmacol, vol. 37 pp. 874-877 (1985).

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[57] **ABSTRACT**

A novel delivery system for targeting drugs to the colon is herein described. The system is a tablet comprised of three parts: 1) an outer enteric coating, 2) an inner semi-permeable polymer membrane containing a plasticizer and 3) a central core comprising swelling excipients and an active ingredient. The novel dosage form described herein will release the drug consistently in the colon by a time-dependent explosion mechanism.

This delivery system is particularly suitable for delivering viral protease inhibitors to the colon.

**14 Claims, 4 Drawing Sheets**